REMARKS

Entry of the foregoing and examination of the above-identified application is respectfully requested. Claims 1-4, 11, 13 and 20 have been deleted in favor of new claims 21-59. Support for the new claims may be found at the very least in the now-deleted claims. No new matter has thus been added by this amendment.

Applicants note with appreciation the alteration of the restriction requirement by the Examiner. The subject matter of claims 1-9, 11-16 and 20 are thus being examined in this application, while claims 10 and 17-19 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-6 and 9 have been rejected under 35 U.S.C. §101 because the claims are allegedly directed to non-statutory subject matter. The Examiner recommends amending the claims to recite "isolated," e.g., in claim 1, an "isolated serine protease." Applicants respectfully traverse this rejection.

The present invention relates to a novel sequence which has been cloned by applicants. As such, the claimed proteins and nucleic acids should be distinguished from nature without requiring the addition of the word "isolated" to the claims. Please note, for example, U.S. Patent Nos. 6,197,925 and 5,354,900, the claims of which are enclosed herewith. In claim 1 of each of these patents, the word "isolated" was not required to define the claimed sequences.

In claim 9, "non-human" has been added prior to "host" to overcome this aspect of the rejection. It is clear from the instant application that applicants' invention does not encompass the breeding of humans. No new matter is thus added by this amendment.

Withdrawal of the rejection of the claims under §101 is thus respectfully requested and believed to be in order.

Claims 1-9 and 11-16 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. This rejection is believed to be overcome by the instant amendment, rewriting the claims.

Moreover, it is believed to be well within the skill in the art to modify the sequences recited in the claims and to test whether the sequence still has serine protease activity, a kringle domain or a scavenger receptor cysteine-rich domain. No undue experimentation would be required by a person skilled in the art to do so. The rejection of the claims on this ground is thus in error.

Withdrawal of this rejection is respectfully requested.

Claims 1-6, 9, 11, 13 and 20 have also been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is believed to be overcome by the instant amendment.

Claims 1-6, 13 and 20 have been rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Gschwend et al. Claims 2, 6, 12 and 14 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Au-Young et al. Claims 2, 6, 12 and 14 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Fujikawa et al. Claims 3, 6, 12 and 15 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wood et al. Claims 3, 6, 12 and 15 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Anderson et al. Claims 4, 6, 12 and 16 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Krieger et al (U.S. Patent No. 5,510,466). Claims 4, 6, 12 and 16 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Krieger et al (U.S. Patent No. 5,624,904). Claims 4, 6, 12 and 16 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Koths et al. Claims 7-9 and 11 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Sonderreger et al in view of Au-Young et al.

It is respectfully submitted that none of the cited references disclose or suggest the novel sequences which are claimed by applications. Since the sequence themselves are novel, the sequences as modified would still be novel. The claims require particular sequences and particular activity, which are not disclosed or suggested by the references.

Withdrawal of these rejections is respectfully requested and believed to be in order.

Further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at 508-339-3684 so that prosecution would be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Donna M. Meuth #39,700
for Donna M. Meuth
Registration No. 36,607

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: March 12, 2001

Attachment to Reply and Amendment dated March 12, 2001

Marked-up Claims 5, 6, 9, and 14-16

5. (Twice Amended) DNA which codes for the serine protease, domain or their partial peptides as claimed [claim 1] in claim 21.

6. (Twice Amended) DNA which codes for a peptide having serine protease, domain or their partial peptide activity, and is hybridizable with DNA that codes for the serine protease, domain or their partial peptides as claimed [claim 1] in claim 21 under stringent conditions.

9. (Amended) A process for preparing serine protease, domain or their partial peptides comprising culturing or breeding a non-human host cell as claimed in claim 8, and recovering serine protease, domain or their partial peptides.

14. (Amended) DNA which codes for the serine protease, domain or their partial peptides as claimed in claim [2] 22.

15. (Amended) DNA which codes for the serine protease, domain or their partial peptide as claimed in claim [3] 23.

16. (Amended) DNA which codes for the serine protease, domain or their partial peptide as claimed in claim [4] 24.

United States Patent 6,197,925
Crabtree , et al. March 6, 2001

NF-AT polypeptides and polynucleotides

Abstract

The invention provides novel polypeptides which are associated with the transcription complex NF-AT, polynucleotides encoding such polypeptides, antibodies which are reactive with such polypeptides, polynucleotide hybridization probes and PCR amplification probes for detecting polynucleotides which encode such polypeptides, transgenes which encode such polypeptides, homologous targeting constructs that encode such polypeptides and/or homologously integrate in or near endogenous genes encoding such polypeptides, nonhuman transgenic animals which comprise functionally disrupted endogenous genes that normally encode such polypeptides, and transgenic nonhuman animals which comprise transgenes encoding such polypeptides. The invention also provides methods for detecting T cells (including activated T cells) in a cellular sample, methods for treating hyperactive or hypoactive T cell conditions, methods for screening for immunomodulatory agents, methods for diagnostic staging of lymphocyte differentiation, methods for producing NF-AT proteins for use as research or diagnostic reagents, methods for producing antibodies reactive with the novel polypeptides, and methods for producing transgenic nonhuman animals.

Inventors: Crabtree; Gerald R. (Woodside, CA); Northrop; Jeffrey P. (Campbell, CA); Ho; Steffan N. (Menlo Park, CA)
Assignee: Sara Lee Corporation (Winston-Salem, NC)
Appl. No.: 260174
Filed: June 13, 1994

Current U.S. Class: 530/300; 435/71; 530/350; 530/351; 536/23; 536/1
Intern'l Class: C07K 005/00; C07K 014/00; G01N 033/53; C07H 021/04
Field of Search: 530/351,350,300 536/23.1 435/320.1,7.1

References Cited [Referenced By]

U.S. Patent Documents

5656452	Aug., 1997	Rao et al.

Foreign Patent Documents

WO 93/04203	Apr., 1993	WO.
WO 94/15964	Jul., 1994	WO.
WO 95/02053	Jan., 1995	WO.

Other References

Bierer, et al. "Two distinct signal transmission pathways in T lymphocytes are inhibited by complexes formed between an immunophilin and either FK506 or rapamycin." PNAS USA 87:9231-9235 (1990).
Clipstone and Crabtree, "Identification of calcineurin as a key signalling enzyme in T-lymphocyte activation" Nature 357:695-697 (1992).
Emmel, et al. "Cyclosproin A specifically inhibits function of nuclear proteins involved in T cell activation" Science 246:1617-1620 (1989).
Flanagan, et al. "Nuclear association of a T-cell transcription factor blocked by FK-506 and cyclosproin A"Nature 352:803-807 (1991).
Israel, Alain. "NF-AT comes under control." Nature 369:443-444 (1994).
Jain, et al. "Nuclear factor of activated T cells contains Fos and Jun." Nature (letters) 356:801-804 (1992).
Jain, et al. "Analysis of the preexisting and nuclear forms of nuclear factor of activated T cells." J. Immunol. 151(2):837-848 (1993).
McCaffrey, et al. "NF-ATp, a T lymphocyte DNA-bindig protein that is a target for calcineurin and immunosuppressive drugs" J Biol Chem 268(5):3747-3752 (1993).
McCaffrey, et al. "Isolation of the cyclosproin-sensitive T cell transcription factor NFATp" Science 262:750-754 (1993).
Northrop, et al. "Characcterization of the nuclear and cytoplasmic components of the lymphoid-specific nuclear factor of activated T cells (NF-AT) complex" J Biol Chem 268(4):2917-2923 (1993).
Northrop, et al. "NF-AT components define a family of transcription factors targeted in T-cell activation." Nature 369:497-502 (1994).
Clipstone, N. and Crabtree, G., "Calcineurin is a key signaling enzyme in T lymphooyte activation and the target of the immunosuppressive drugs cyclosporin A and FK506", Ann. N.Y. Acad. Sci., 696: 20-30 (1993).
Crabtree, G. And Clipstone, N., "Signal transmission between the plasma membrane and nucleus of T lymphocyte",Ann. Rev. Biochem., 63: 1045-1083 (1994).
Ho, S. et al., Cloning and characterization of NF-AT.sub.c and NF-AT.sub.p :the cytoplasmic components of NF-AT, Adv.Exp. Med. Biol. 365:167 (1994).
Jain, J. et al., "The T cell transcription factor NF-AT.sub.p is a substrate for calcineurin and interacts with Fos and Jun", Nature, 365(6444):352-355 (1993).
McCaffrey, P. et al., "Isolation of the cyclosporin-sensitive T cell transcription factor NF-AT.sub.p ", Science, 262: 750-754 (1993).
Verweij, C. et al., "Cell type and activation requirements for NFAT-1 transcriptional activity determined by a new method using transgenic mice to assay transcriptional activity . . .". J. Biol. Chem., 265 (26): 15788-15795 (1990).
Rao, A., "NF-AT.sub.p : a transcription factor required for the co-ordinate induction of several cytokine genes", Immunology Today, 15(6): 274-281 (1994).
Crabtree G. "Pathways of T lymphocyte activation" Abstract of NIH Grant No. R01CA39612 (1988).
Crabtree G. "Pathways of T lymphocyte activation" Abstract of NIH Grant No. R01CA39612 (1991).
Shaw et al. "Identification of a putative regulator of early T cell activation genes" Science 241: 202 (1988).
U.S. application N . 08/145,006, Rao et al., filed Nov. 15, 1993.
U.S. application No. 08/017,053, Rao et al., filed Feb. 11, 1993.
U.S. application No. 08/006,067, Rao et al., filed Jan. 15, 1993.
U.S. application No. 08/088,483, Aral et al., filed Aug. 30, 1993.
U.S. application No. 08/088,483, Aral et al., filed Jul. 6, 1993.
U.S. application No. 08/099,998, Arai et al., filed Jul. 30, 1993.

U.S. application 08/148,061, Arai et al., filed Nov. 5, 1993.
Crabtree G. "Contingent genetic regulatory events in T lymphocyte activation" Science 243:355 (1989).
Schmidt et al. "Inducible nuclear factor binding to the kB element of the human immunodeficiency virus enhancer in T cells can be blocked by cyclosporin A in a signal-dependent manner" J. Virol. 64:4037 (1990).
Mattila et al. "The actions of cyclosporin A and FK506 suggest a novel step in the activation of T lymphocytes" EMBO J. 9:4425 (1990).
Banerji et al. "The immunosuppressant FK-506 specifically inhibits mitogen induced activation of the Interleukin-2 promoter and the isolated enhancer elements NFIL-2A and NF-AT1" Mol. Cell. Biol. 11: 4074 (1991).
Riegel et al. "Nuclear events after activation of CD4+CD8+ thymocytes" J. Immunol. 144:3611(1990).

Primary Examiner: Schwartzman; Robert A.
Assistant Examiner: Wang; Andrew

Goverment Interests

STATEMENT OF RIGHTS

This invention was made in the course of work supported by the U.S. Government and Howard Hughes Medical Institute, which may have certain rights in this invention.

Parent Case Text

This application is a continuation-in-part of U.S. Ser. No. 08/124,981 filed Sep. 20, 1993 which is a continuation-in-part of U.S. application Ser. No. 07/749,385, entitled "Screening Methods for Immunosuppressive Agents", by G. R. Crabtree and W. M. Flanagan, which was filed on Aug. 22, 1991, now U.S. Pat. No. 5,837,840 now abandoned.

Claims

What is claimed is:

1. A polypeptide whose amino acid sequence is identical to amino acids 1-418 of FIG. 1 (SEQ ID NO:38).

2. An isolated polypeptide which is encoded by a nucleic acid which hybridizes specifically to a nucleic acid having the nucleotide sequence set forth in SEQ ID NO: 45, wherein the isolated polypeptide has one or more of the following biological activities:

(i) binds a nuclear component of an NF-AT complex;

(ii) binds calcineurin;

(iii) directs nuclear localization upon T cell activation;

(iv) activates gene transcription;

(v) binds DNA when reconstituted with an NF-AT nuclear c mpon nt;

(vi) competitively antagonizes wild-type NF-ATc;

(vii) modulates an immune response; and

(viii) cross-reacts with an antibody which binds to a polypeptide consisting of SEO ID NO: 38.

3. The polypeptide of olaim 2, which binds AP-1.

4. The polypeptide of claim 2, which activates transcription of the IL-2 gene.

5. The polypeptide of claim 2, which has DNA binding activity when complexed with AP-1.

6. The polypeptide of claim 2, which binds the IL-2 enhancer.

7. The polypeptide of claim 2, which is a mammalian NF-AT protein.

8. The polypeptide of claim 2, which is a human NF-AT protein.

9. The polypeptide of claim 2, which is a fusion protein.

10. The polypeptide of olaim 2, which comprises at least 25 amino acids.

11. The polypeptide of claim 10, which comprises at least 25 amino acids of SEQ ID NO: 38.

12. The polypeptide of claim 10, which comprises at least 50 amino acids.

13. The polypeptide of claim 12, which comprises at least 50 amino acids of SEQ ID NO: 38.

14. The polypeptide of claim 2, which is a naturally-occurring NF-AT polypeptide.

15. The polypeptide of claim 2, which comprises a Rel Similarity Region.

16. The polypeptide of claim 15, wherein the Rel Similarity Region comprises amino acids 418-710 of SEQ ID NO: 38.

17. The polypeptide of olaim 2, which is a dominant negative mutant of NF-AT.

18. The polypeptide of claim 2, which comprises amino acids 1-418 of SEQ ID NO: 38.

19. The polypeptide of claim 2, which comprises the amino acid sequence set forth in SEQ ID NO: 38.

20. The polypeptide of claim 19, which consists of the amino acid sequence set forth in SEQ ID NO: 38.

21. The polypeptide of claim 2, which is phosphorylated.

22. The polypeptide of claim 2, which is encoded by a nucleic acid which hybridizes specifically to a nucleic acid having the nucleotide sequence set forth in SEQ ID NO: 45 under stringency conditions of 5.times. SSC at 42.degree. C.

23. The polypeptide of claim 2, which is enc ded by a nucleic acid which hybridizes specifically to a nucleic acid having the nucleotide s quence set forth in SEQ ID NO: 45 under stringency conditions of 5.times. SSC at 70.degree. C.

24. The polypeptide of claim 6, which binds the IL-2 enhancer with an affinity of at least about 10.sup.-6 M.sup.-1.

25. The polypeptide of claim 2, further comprising a heterologous polypeptide.

Description

FIELD OF THE INVENTION

The invention provides novel polypeptides which are associated with the transcription complex NF-AT, polynucleotides encoding such polypeptides, antibodies which are reactive with such polypeptides, polynucleotide hybridization probes and PCR amplification probes for detecting polynucleotides which encode such polypeptides, transgenes which encode such polypeptides, homologous targeting constructs that encode such polypeptides and/or homologously integrate in or near endogenous genes encoding such polypeptides, nonhuman transgenic animals which comprise functionally disrupted endogenous genes that normally encode such polypeptides, and transgenic nonhuman animals which comprise transgenes encoding such polypeptides. The invention also provides methods for detecting T cells (including activated T cells) in a cellular sample, methods for treating hyperactive or hypoactive T cell conditions, methods for screening for immunomodulatory agents, methods for diagnostic staging of lymphocyte differentiation, methods for producing NF-AT proteins for use as research or diagnostic reagents, methods for producing antibodies reactive with the novel polypeptides, and methods for producing transgenic nonhuman animals.

BACKGROUND OF THE INVENTION

The immune response is coordinated by the actions of cytokines produced from activated T lymphocytes. The precursors for most T lymphocytes arise in the bone marrow and migrate to the thymus where they differentiate and express receptors capable of interacting with antigen. These differentiated T lymphocytes then migrate to the peripheral lymphoid organs where they remain quiescent until they come in contact with the cognate antigen. The interaction of antigen with the antigen receptor on T lymphocytes initiates an ordered series of pleiotropic changes: a process denoted as T lymphocyte activation. T lymphocyte activation is a 7 to 10 day process that results in cell division and the acquisition of immunological functions such as cytotoxicity and the production of lymphokines that induce antibody production by B lymphocytes and control the growth and differentiation of granulocyte and macrophage precursors. The cytokines produced by activated T lymphocytes act upon other cells of the immune system to coordinate their behavior and bring about an effective immune response.

The initiation of T lymphocyte activation requires a complex interaction of the antigen receptor with the combination of antigen and self-histocompatibility molecules on the surface of antigen-presenting cells. T lymphocytes may also be activated by relatively simple stimuli such as the combination of a calcium ionophore (e.g., ionomycin) and an activator of protein kinase C, such as phorbol myristate acetate (PMA). Several lectins, including phytohemagglutinin (PHA) may also be used to activate T cells (Nowell (1960) Cancer Res. 20: 462).

T lymphocyte activation involves the specific regulation of particular subsets of genes. The transcriptional regulation characteristic of T cell activation b gins minutes after the antigen encounter and c ntinues until at least 10 days later. The T lymphocyte activation genes can be grouped according to the time after stimulation at which each gene is transcrib d. Early genes are the first subset of T lymphocyte activation genes that is expressed during the activation process. Expression of the early genes triggers the transcriptional modulation of subsequent genes in the activation pathway. Because of the critical rol of the T lymphocyte

US PATENT & TRADEMARK OFFICE
PATENT FULL TEXT AND IMAGE DATABASE

United States Patent 5,354,900
Matsuo , et al. October 11, 1994

An H-ANP peptide, pharmaceutical composition and method of use

Abstract

There are disclosed a new peptide .alpha.-hANP of the following structure: ##STR1## and acid addition salt thereof; a diuretic composition and a hypotensor composition containing the .alpha.-hANP or an acid addition salt thereof; and processes for the production thereof.

Inventors: Matsuo; Hisayuki (6653, Ooaza-kihara, Kiyotake-cho, Miyazaki-gun, Miyazaki-ken, JP); Kangawa; Kenji (Miyazaki, JP)
Assignee: Suntory Limited (Osaka, JP); Matsuo; Hisayuki (Miyazaki, JP)

Appl. No.: 685151
Filed: December 21, 1984

Foreign Application Priority Data

Dec 26, 1983[JP] 58-243675

Current U.S. Class: 514/12; 514/13; 530/324; 530/325
Intern'l Class: A61K 037/02; C07K 007/10
Field of Search: 260/112.5 R 514/11,12,13 530/324,325

References Cited [Referenced By]

U.S. Patent Documents

4496544	Jan., 1985	Needleman	514/13.
4508712	Apr., 1985	Needleman	514/11.

Other References

Life Sci. vol. 33, 297-302 (1983).
Biochem. & Biophys Res. Commun. 118, 131-139 (1984).
Science (1983) 71-73 vol. 221.
Biochem. & Biophys. Res. Commun. 122 (1984) 1076-1082.
Proc. of the Soc. Exper. Biol. Med. 170, 133-138 (1982).
Biochem. & Biophys. Res. Commun. (1983) 859-865 vol. 117, No. 3.
Can. Journal of Phys. & Pharm. 61, No. 2 (1983) 127-130.
Can. Journal of Phys. & Pharm. 60, No. 3, (1982) 324-330.
Life Sci. vol. 28, 89-94 (1980).
Jamieson, J. D. and Palade, G. E., "Specific Granules in Atrial Muscle Cells", The Journal of Cell Biology, vol. 23 (1964), pp. 151-172.
de Bold, A. J. et al. "A Rapid and Potent Natriuretic Response to Intravenous Injection of Atrial Myocardial Extract in Rats", Life Sciences, vol. 28 (1981), pp. 89-94.
Keeler, R., "Atrial Natriuretic Factor has a Direct, Prostaglandin-independent Action on Kidneys", Can. J. Physiol. Pharmacol., vol. 60 (1982) pp. 1078-1082.
Currie, M. G. et al. "Bioactive Cardiac Substances: Potent Vasorelaxant Activity in Mammalian Atria", Science, vol. 221 (1983), pp. 71-73.

Primary Examiner: Lee; Lester L.
Attorney, Agent or Firm: Burns, Doane, Swecker & Mathis

Claims

We claim:

1. A peptide .alpha.-hANP having the following formula: ##STR7## wherein 1 and 2 are directly bonded, Asp represents L-

aspartic acid, Asn represents L-asparagine, Ala represents L-alanine, Arg represents L-arginine, Ile represents L-isoleucine, Gly represents glycine, Glu represents L-glutamic acid, Gln represents L-glutamine, Cys represents together with —S— 1/2 L-cysteine, Ser represents L-serine, Tyr represents L-Tyrosine, Phe represents L-phenylalanine, Met represents L-methionine, and Leu represents L-leucine, and the amino acid chain has an amino-termical at the left end, and carboxy-terminal at the right end, and acid addition salts thereof.

2. A pharmaceutical composition for use as a diuretic or antihypertensive agent comprising a diuretically effective amount or an antihypertensively effective amount of a peptide .alpha.-hANP having the following formula: ##STR8## or an acid addition salt thereof with a conventional pharmaceutical additive.

3. The pharmaceutical composition according to claim 2, wherein the composition is a solution for parenteral administration and the conventional pharmaceutical additive is a buffer, an osmotic pressure adjusting agent or a preservative, or a combination thereof.

4. The pharmaceutical composition according to claim 2, wherein the composition is a solution for parenteral administration and contains about 0.000005 to 5% of the .alpha.-hANP.

5. The pharmaceutical composition according to claim 2, wherein the composition is in a lyophylized form.

6. A method for promoting diuresis comprising administering a diuretically effective amount of a peptide .alpha.-hANP having the following formula: ##STR9## or an acid addition salt thereof with a conventional pharmaceutical additive.

7. The method according to claim 6, wherein the conventional pharmaceutical additive is a buffer, an osmotic pressure adjusting agent or a preservative, or a combination thereof.

8. The method according to claim 6, wherein about 0.000005 to 5% of the .alpha.-hANP based on the weight of the .alpha.-hANP and additive is administered parenterally.

9. A method for lowering blood pressure comprising administering an antihypertensively effective amount of a peptide .alpha.-hANP having the following formula: ##STR10## or an acid addition salt thereof with a conventional pharmaceutical additive.

10. The method according to claim 9, wherein the conventional pharmaceutical additive is a buffer, an osmotic pressure adjusting agent or a preservative, or a combination thereof.

11. The method according to claim 9, wherein about 0.000005 to 5% of the .alpha.-hANP based on the weight of the .alpha.-hANP and additive is administered parenterally.

12. A peptide .alpha.-hANP in isolated form having the following formula: ##STR11## wherein 1 and 2 are directly bonded, Asp represents L-aspartic acid, Asn represents L-asparagine, Ala represents L-alanine, Arg represents L-arginine, Ile represents L-isoleucine, Gly represents glycine, Glu represents L-glutamic acid, Gln represents L-glutamine, Cys represents together with —S— 1/2 L-cystine, Ser represents L-serine, Tyr represents L-tyrosine, Phe represents L-phenylalanine, Met represents L-methionine, and Leu represents L-leucine, and the amino acid chain has an amino-terminal at the left end, and carboxy-terminal at the right end, and acid addition salts thereof.

Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a novel peptide, a process for the production thereof, and a pharmaceutical composition containing the novel peptide as a diuretic or hypotensor.

2. Description of the Related Art

A normal regulation of the blood pressure in a human body is important for the maintenance of personal health, and various physical and humoral factors contribute to this regulation of the blood pressure. The physical factors include, for example, output, and the elasticity of the walls of blood vessels, etc. The humoral factors include, for example, the renin-angiotensin-aldosterone system, catecholamines, prostaglandins, kinin-kallikrein system, and natriuretic hormones including ouabain-like substances. Herein the term "natriuretic" will denote selective excretion of sodium cation relating to potassium cation.

Granules morphologically similar to granules present in peptide hormone-producing cells are found in human atrium (J. D. Jamieson and G. E. Palade, J. Cell Biol., 23, 151, 1964). A homogenate of rat atrium and granules contained therein are known to show natriuretic action in rats (A. J. DeBold et. al., Life Science, 28, 89, 1981; R. Keeller, Can. J. Physiol. Pharmacol., 60, 1078, 1982). Recently, Mark G., Currie S. et al. suggested peptide-like substances with a molecular weight of 20,000 to 30,000, or not more than 10,000, present in atrium of humans, rabbits, swine, and rats, and having natriuretic action (Science, 221, 71~73, 1983).

SUMMARY OF THE INVENTION

The present invention provides a new peptide having natriuretic action and hypotensive of antihypertensive action. The peptide according to the present invention is hereinafter referred to as ".alpha.-human atrial natriuretic polypeptide" and abbreviated as ".alpha.-hANP".